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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/668,749	09/23/2003	Hui Wang	10030304-1	2131

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AGILENT TECHNOLOGIES, INC.  
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EXAMINER	
CLOW, LORI A	
ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 11/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

10/668,749

Applicant(s)

WANG, HUI

Examiner

Lori A. Clow, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 07 September 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-21 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-21 is/are rejected.
- 7) ☒ Claim(s) 18 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

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### **DETAILED ACTION**

Applicants' response, filed 7 September 2006, has been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claims 1-21 are currently pending.

#### **Claim Objections**

Claim 18 is objected to because of the following informalities: Claim 18 recites, "determine a ratio of phosphorylated target polynucleotide to non-phosphorylated target polynucleotides". The claim phrase contains a grammatical error and should read, "determine a ratio of phosphorylated target polynucleotides". Appropriate correction is required.

#### **Claim Rejections - 35 USC § 101**

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 15-21 remain rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The "system for performing nanopore data analysis" does not generate an outcome which is concrete, tangible, and useful, nor does the system result in a physical transformation of matter. Applicant argues that the claims have been amended to recite useful, concrete and tangible results including: "to aid in a determination of at least one of the following:

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phosphorylation state of the target polynucleotides, length diversity among polynucleotides present in a sample, chemical integrity of the target polynucleotides, and a ratio of target polynucleotides to non-target polynucleotides in the sample”.

This is not persuasive. The instant system is operative to generate nanopore data points, form a distribution pattern of the data points, and analyze a distribution of the target polynucleotide data points. The system is merely operative to perform *in silico* data steps and is not limited to any hardware elements or combination of software and hardware elements such that it is interpreted to be a physical article of manufacture. The system does not provide a result to a user that is concrete, tangible and useful. Further, the system does not provide for a physical transformation of matter, such that the claims would be statutory. The rejection is hereby maintained.

Note: The rejection with regard to claims 1-14 has been withdrawn in view of the amendments to the claims that make clear that the method step includes a physical transformation of matter, i.e. providing a sample including target polynucleotides to a nanopore device and generating data points from the samples traversing an aperture of the nanopore.

#### **Claim Rejections - 35 USC § 112**

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This rejection is necessitated by amendment to the claims.

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Claims 1 and 15 recites “to aid in the determination of “. It is unclear if this is intended to be an active method step of actually “determining” the phosphorylation state of the target polynucleotides, the length diversity, chemical integrity or ratio or target to non-target or if this is an intended use of the method. Clarification is requested.

### **Claim Rejections - 35 USC § 102**

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 10, 12, 15, 16, 20, and 21 remain rejected under 35 U.S.C. 102(a) as being anticipated by WO 02/42496 (Haussler et al.), for the reasons set forth in the previous Office action and re-iterated below.

In regard to claims 1, 2, 10, 15, 16, 20 and 21 Haussler teaches methods and devices for characterizing DNA molecules using a nanopore device. The characterization of nucleic acids through the nanopore device may include assigning a signature to the nucleic acid, wherein the signature may take various forms, including raw data values, manipulated sets of data values, and the like (page 8, lines 17-24). The signature may be screened against a reference signature to identify and observed signature (page 15, lines 13-18). The analysis includes distribution analysis (page 23-29 (Gaussian curve generation). The system may be automated and include computing means made of hardware and software (page 18, lines 1-10).

***Response to Applicant's Arguments with regard to Haussler et al.***

Applicant argues that “the independent claims 1 and 15 have been amended to recite the features of analyzing a distribution of polynucleotide data points in the distribution pattern to **aid in a determination of at least one of the following: phosphorylation state of the target polynucleotides, length diversity among polynucleotides present in a sample, chemical integrity of the target polynucleotides, and a ration of target polynucleotides to non-target polynucleotides in the sample**”. Applicant contends that Haussler “merely discloses identifying one particular nucleic acid in a sample and not any of the features recited above”.

This is not persuasive. Haussler et al. teach that various lengths of nucleic acid molecules may be characterized (page 8, lines 9 and 10). Further, with regard to analysis of length diversity as instantly claimed, Haussler et al. teach that “DNA hairpins with stems that ranged in length from 3 to 9 base-pairs” were tested for analysis of the accuracy of the method, with a result showing that each base pair addition resulted in measurable increase in blockade shoulder lifetime for each additional base pair (page 33, lines 33-34 to page 34, lines 1-4). Thus, Haussler et al. teach nanopore analysis to determine length diversity, as set forth in the instant claims.

Further, Haussler et al. teach the detection of DNA damage (e.g. depurination and thymine dimerization) using the above method (page 15, lines 27-33). Therefore, Haussler et al. teach the determination of chemical integrity of a DNA molecule, as is instantly claimed.

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Claims 1, 2, 10, 12, 15, 16, 20 and 21 remain rejected under 35 U.S.C. 102(b) as being anticipated by Meller et al. (PNAS (2000) Vol. 97, No. 3, pages 1079-1084), as set forth in the previous Office Action and re-iterated below.

In regard to claims 1 and 15, Meller teaches introducing DNA samples to a nanopore device whereby data are analyzed via software to yield a distribution pattern (page 1080, column 1; Figure 2; page 1082, column 1, 2<sup>nd</sup> paragraph).

In regard to claims 2 and 10, Meller teaches the analysis of data clusters within a distribution (page 1080, column 1, Results and Discussion (i) and (ii)).

In regard to claim 12, Meller teaches the distribution as indicative of polymers of the same length (page 1081, column 1, paragraph 2).

In regard to claim 20, Meller teaches the storage of nanopore data (page 1080, column 1, paragraph 1).

In regard to claim 21, Meller teaches a means for analyzing the distribution data (page 1080, column 1, paragraph 1).

***Response to Applicant's Arguments with regard to Meller et al.***

Applicant argues that “the independent claims 1 and 15 have been amended to recite the features of analyzing a distribution of polynucleotide data points in the distribution pattern to **aid in a determination of at least one of the following: phosphorylation state of the target polynucleotides, length diversity among polynucleotides present in a sample, chemical integrity of the target polynucleotides, and a ration of target polynucleotides to non-target polynucleotides in the sample**”. Applicant contends that Meller “discloses the distribution as indicative of polymers of the same length”.

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This is not persuasive. While the Examiner contends that Meller does disclose the assessment of polymers of the same length that vary only in sequence composition, Meller also teaches the use of the method to distinguish chemical integrity. For example, Meller et al. teach temperature range variation effects on different polymer types, therefore teaching the method to determine chemical integrity.

The rejections are hereby maintained.

### **Conclusion**

No claims are allowed.

The outstanding claim objections have been withdrawn in view of the amendments to the claims.

The outstanding rejection under 35 USC 101, non-statutory subject matter with regard to claims 1-14 has been overcome. See note above.

The outstanding rejection under 35 USC 112, 1<sup>st</sup> paragraph, scope of enablement, has been withdrawn in view of the amendments to the claims that include polynucleotide targets only.

The outstanding rejections under 35 USC 112, 2<sup>nd</sup> paragraph have been withdrawn in view of the amendments to the claims. The newly applied rejections under 112, 2<sup>nd</sup> are necessitated by amendment to the claims.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).



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A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

### **Inquiries**

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The Central Fax Center Number is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lori A. Clow, Ph.D., whose telephone number is (571) 272-0715. The examiner can normally be reached on Monday-Friday from 10 am to 6:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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November 18, 2006

Lori A. Clow, Ph.D.

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*Lori A. Clow*  
*Patent Examiner*  
*11/17/06*